PATENT
Customer No. 22,852
Attorney Docket No. 06843.0035-00000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Jean-Michel DAYER et al.	)	Group Art Unit: 1644
	)	
Application No.: 09/803,918	)	Examiner: Phuong N. Huynh
	)	
Filed: March 13, 2001	)	
	)	
For: APO-A-I REGULATION OF T-CELL SIGNALING	)	Confirmation No.: 8922
	)	

Attention: Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPEAL BRIEF UNDER BOARD RULE § 41.37

In support of the Notice of Appeal filed June 30, 2005, and further to Board Rule 41.37, Appellant presents this brief and enclose herewith a check for the fee of $500.00 required under 37 C.F.R. § 1.17(c).

This Appeal Brief is being filed concurrently with a Petition for an Extension of Time for five months, and the appropriate fee.

This Appeal responds to the December 30, 2004, final rejection of claims 9, 10, 15, 16, 36-43, and 46-49.

If any additional fees are required or if the enclosed payment is insufficient, Appellants request that the required fees be charged to Deposit Account No. 06-0916.

Table of Contents

Real Party In Interest 3

Related Appeals and Interferences 4

Status Of Claims 5

Status Of Amendments 6

Summary Of Claimed Subject Matter 7

Grounds of Rejection 8

Argument 9

A. The Specification Enables AFTI Polypeptides Consisting Essentially of the Recited Sequences 10

B. The Specification Enables AFTI Polypeptides Having Conservative Amino Acid Substitions 12

Conclusion 19

Claims Appendix to Appeal Brief Under Rule 41.37(c)(1)(viii) 20

Evidence Appendix to Appeal Brief Under Rule 41.37(c)(1)(ix) 32

Related Proceedings Appendix to Appeal Brief Under Rule 41.37(c)(1)(x) 33

Real Party In Interest

The assignees, Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320, and the University of Geneve, 24 Rue Micheli-Du-Crest, 1211 Geneve 14, Switzerland, are the real parties in interest.

Related Appeals and Interferences

There are currently no other appeals or interferences, of which Appellants, Appellants' legal representative, or Assignees are aware, that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

Status Of Claims

Claims 1-16 and 18-61 are pending in the application. Claims 9, 10, 15, 16, 36-43, and 46-49 are rejected. Claims 1-8, 11-14, 18-35, 44, 45, and 50-61 are withdrawn from consideration as allegedly being drawn to nonelected inventions. Claim 17 has been cancelled. The rejection of claims 9, 10, 15, 16, 36-43, and 46-49 is appealed.

Status Of Amendments

No amendments were filed subsequent to the final rejection.

Summary Of Claimed Subject Matter

The claims on appeal encompass polypeptides called apolipoprotein A-I ("apo-A-I") fragment T-cell activation inhibitors ("AFTIs"), which in certain embodiments encompassed by claim 15 consist essentially of portions of SEQ ID NO:2. *See* Specification, page 5, lines 14-16. In other embodiments encompassed by claim 15, the AFTI polypeptides consist essentially of portions of SEQ ID NO:2 having one or more conservative amino acid substitutions wherein the polypeptide inhibits tumor necrosis factor or interleukin-1 production from monocytes. *See, e.g.*, Specification, page 5, lines 24-29; page 98, line 18 through page 99, line 9.

The claims also encompass nucleic acid molecules, which in certain embodiments encompassed by claim 16 consist essentially of portions of SEQ ID NO:1, encoding AFTI polypeptides. *See* Specification, page 4, lines 4-26. (Note that the nucleotide numbers recited by subparts (a), (c), and (e) of original claims 9 and 10 were incorrect as originally filed due to a clerical error. The specification, and those subparts of claims 9 and 10, were corrected by Appellants' Amendment and Response to Office Action filed September 24, 2004). In other embodiments encompassed by claim 16, the nucleic acid molecules encode an AFTI polypeptide having one or more conservative amino acid substitutions wherein the polypeptide inhibits tumor necrosis factor or interleukin-1 production from monocytes. *See, e.g.*, Specification, page 6, lines 20-27; page 98, line 18 through page 99, line 9.

In certain embodiments encompassed by claims 9 and 10, the invention provides a process for making AFTI polypeptides in either eukaryotic or prokaryotic cells, respectively. *See, e.g.*, Specification, page 102, line 11 through page 104, line 3.

Grounds of Rejection

Claims 9, 10, 15, 16, 36-43, and 46-49 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification.

Argument

The Examiner contends that the specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with claims 9, 10, 15, 16, 36-43, and 46-49 and therefore rejects those claims under 35 U.S.C. § 112, first paragraph. Office Action mailed December 30, 2004 ("Office Action"), at 4. The Examiner acknowledges that the specification enables one skilled in the art to make and use:

a. AFTI-like polypeptides *consisting of* any of the amino acid sequences set forth in subparts (a) to (e) of claim 15, *id.* at 3;

b. AFTI-like polypeptides encoded by a nucleic acid molecule *consisting of* any of the nucleotide sequences set forth in subparts (1) to (5) of claim 16, *id.*;

c. the compositions according to claims 36-39 comprising the above-mentioned AFTI-like polypeptides, *id.* at 3-4;

d. the above-mentioned AFTI-like polypeptides covalently modified with polymers as recited by claims 40-43, *id.* at 4; and

e. fusion proteins comprising the above-mentioned AFTI-like polypeptides as recited by claims 47-49, *id.*

The Examiner also acknowledges that the specification enables one skilled in the art to perform the processes recited by claim 9 and 10 where the vector comprises a nucleic acid molecule *consisting of* any of the nucleotide sequences set forth in subparts (a) to (i) of those claims. *Id.* at 2-3.

In fact, there are only two questions presented by this appeal:

1. Does the specification enable one skilled in the art to make and use AFTI-like polypeptides *consisting essentially of* the amino acid sequences set forth in subparts (a) to (e) of claim 15 or encoded by a nucleic acid molecule *consisting essentially of* any of the nucleotide sequences set forth in subparts (1) to (5) of claim 16?
2. Does the specification enable one skilled in the art to make and use the above-mentioned AFTI-like polypeptides having one or more conservative amino acid substitutions?

Appellants contend that the answer to both questions is "yes."

A. The Specification Enables AFTI Polypeptides "Consisting Essentially of" the Recited Sequences

The phrase "'consisting essentially of' limits the scope of a claim to the specified materials or steps 'and those that do not materially affect the basic and novel characteristic(s)' of the claimed invention." M.P.E.P. § 2111.03 (citing *In re Herz*, 537 F.2d 549, 551-52 (C.C.P.A. 1976)) (emphasis in original); *see also Regents of the Univ. of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1573 (Fed. Cir. 1997) (noting that the Examiner was correct in interpreting a claim reciting "human [proinsulin] ***consisting essentially of*** a plus strand having the sequence [nucleotides that encode human proinsulin]" to exclude fusion proteins (emphasis in original)). M.P.E.P § 2111.03 provides a single exception to this rule, advising that "[f]or the purpose of searching for and applying prior art under 35 U.S.C. § 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to 'comprising.'"

That exception is not applicable here, where the rejection is not based on prior art. Moreover, even if the exception could apply, the specification and claims clearly do identify the basic and novel characteristics of the invention: the claimed AFTI-like polypeptides inhibit tumor necrosis factor (TNF) or interleukin-1 (IL-1) production by monocytes. Polypeptide fragments that do not have this property are not encompassed by the claims.

In addition, the specification makes it clear that the phrase "consisting essentially of" does not mean the same thing as the phrase "comprising." In fact, Appellants have distinguished between two embodiments: 1) "an isolated polypeptide *consisting essentially of* an amino acid sequence selected from . . ." (e.g., page 4, line 27, to page 5, line 13 (emphasis added)); and 2) "an isolated polypeptide *comprising* the amino acid sequence selected from . . ." (e.g., page 5, line 24, to page 6, line 15 (emphasis added)).

Nevertheless, the Examiner persists in stating that "the term 'consisting essentially of' is still open-ended, albeit the sequence is not the same length as set forth in SEQ ID NO: 2."[1] Office Action at 8. Based on her construction of the transitional phrase, the Examiner concludes that claims 9, 10, 15, 16, 36-43, and 46-49 encompass an "indefinite number of undisclosed polypeptide[s] and the corresponding nucleotides for the additional amino acids." (Office Action mailed October 22, 2002, at 7; Office Action at 8). The Examiner provides no basis for her conclusion.

---

[1] Appellants presume the Examiner means *because* "the sequence is not the same length as set forth in SEQ ID NO: 2." The word "albeit" means "although" and makes no sense in this context.

Properly construed, the transitional phrase "consisting essentially of" limits the scope of claims 9, 10, 15, 16, 36-43, and 46-49 to sequences that do not "materially affect the basic and novel characteristic(s)" of the claimed AFTI-like polypeptide fragments. Therefore, those claims do not encompass an "indefinite number" of polypeptides and nucleic acids, as asserted by the Examiner. Instead, only the specific recited polypeptide and nucleic acid sequences as well as those sequences that do not have materially different properties are within the scope of claims 9, 10, 15, 16, 36-43, and 46-49. In view of the breadth of knowledge concerning apo A-I structure and function (see below), the Examiner has provided no reason to conclude that one skilled in the art would encounter any difficulty in determining what amino acids might be added to specific AFTI-like polypeptide fragments without materially modifying their properties.

B. The Specification Enables AFTI Polypeptides Having Conservative Amino Acid Substitutions

In response to the Appellants' arguments that the phrase "consisting essentially of" is not open-ended, the Examiner contended, *inter alia*, that "there is insufficient guidance as to the structure of any apo-A-I fragment T-cell activation inhibitor-like polypeptide fragment having one or more conservative substitution without the amino acid sequence and/or the corresponding nucleotide sequence." Office Action at 8. Appellants respectfully disagree.

As an initial point, Appellants note that amendments to obviate the enablement rejection of the claims presently appealed were discussed during a telephone interview between the Examiner and Appellants' representative on May 17, 2004. *See*

Examiner's Interview Summary, mailed May 20, 2004. Appellants contend that the claim amendments filed with the Amendment and Response to Office Action on September 24, 2004, were sufficient to overcome the enablement rejection. Appellants further respectfully assert that, during the telephone interview, "[t]he Examiner acknowledged that claims encompassing one or more conservative amino acid substitutions were enabled." Amendment and Response to Office Action filed September 24, 2004, at page 23. Yet in the present Office Action, it appears the Examiner has reversed her prior position, and furthermore, has provided no explanation for the reversal.

In any case, Appellants submit that the claims are fully enabled for AFTI polypeptides consisting essentially of the denominated sequences and consisting essentially of those sequences having conservative amino acid substitutions. The test for enablement is whether "the experimentation needed to practice the invention is undue or unreasonable." M.P.E.P. § 2164.01, *citing Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916). The factors to consider in determining whether the experimentation is undue are the *Wands* factors, which include (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. M.P.E.P. § 2164.01(a); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

According to the Examiner, "the factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient

working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention." Office Action, mailed October 22, 2002, at page 6; Office Action at pages 4-5. However, the M.P.E.P. clearly states that "[t]he examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole." M.P.E.P. § 2164.01(a). Consideration of each of the *Wands* factors supports the conclusion that the full scope of the claims is enabled. Each factor is considered below:

(a) The Breadth of the Claims

As discussed at length above, the claims are not unduly broad for reciting the transitional phrase "consisting essentially of."

(b) The Nature of the Invention

The invention relates to polypeptides derived from a well known and thoroughly characterized human protein Apo-A-I that have an easily assayed activity, inhibiting TNF or IL-1 production by monocytes. Exemplary polypeptide and nucleotide sequences are provided, as are methods for assaying TNF and IL-1 production by monocytes.

(c) The State of the Prior Art

The amount of knowledge in the state of the art is extensive, both with respect to the field of apo-A-I, which includes AFTI, and with respect to conservative amino acid substitutions. As Appellants previously pointed out, a search of the PubMed database by Appellants' representative showed that nearly 5000 scientific papers concerning apo-A-I had been published before the filing date of the present application. In addition, a

search of the Genbank database for "apolipoprotein A-I" returned 452 protein and 1484 nucleotide sequences from a wide variety of species. Appellants' Response to Office Action, filed April 16, 2003, page 13. In addition, the amount of knowledge in the art regarding conservative amino acid substitutions is extensive. Certain of that art is discussed in the specification at pages 23-31. On those same pages, the specification also refers to numerous scientific publications that provide further details concerning conservative amino acid substitutions. *Id.* Accordingly, the above discussion demonstrates that the amount of knowledge in the fields of apo-A-I and conservative amino acid substitutions is extensive.

(d) The Level of One of Ordinary Skill

The level of one of ordinary skill in the relevant art is very high. Most have doctoral degrees and additional advanced training (e.g., postdoctoral fellowships).

(e) The Level of Predictability in the Art

The level of predictability in the art of conservative amino acid substitutions is high. "The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art." M.P.E.P. § 2164.03. The specification discloses, *inter alia*, certain amino acid sequences of AFTI-like polypeptides, certain assays for inhibition of TNF and IL-1 production by monocytes, and certain exemplary results. *See, e.g.*, SEQ ID NO:2, and Example 1. The specification also provides guidance on conservative amino acid substitutions, in addition to referring to numerous scientific publications, which provide further details on

conservative amino acid substitutions, as discussed above. Accordingly, one skilled in the art would be able to readily determine appropriate conservative amino acid substitutions of the disclosed amino acid sequences of AFTI-like polypeptides that would, with a high degree of predictability, maintain the disclosed function of inhibiting TNF and IL-1 production by monocytes.

(g) The Existence of Working Examples

The working examples provide assays for inhibition of TNF and IL-1 production by monocytes by AFTI-like polypeptides. Applicants disclose eight nucleic acid sequences (nucleotides 25 to 113, 25 to 144, 25 to 194, 73 to 113, 73 to 582, 73 to 432, 156 to 257, and 466 to 801 in SEQ ID NO:1) and five amino acid sequences (residues 25 to 113, 25 to 144, 25 to 194, 73 to 113, and 156 to 267 in SEQ ID NO:2) that encode or are AFTI polypeptide fragments according to the invention. One skilled in the art would be able to make AFTI-like polypeptides consisting essentially of these sequences or with conservative amino acid changes and to determine whether such polypeptides inhibit TNF and/or IL-1 production by monocytes by using the disclosure and the knowledge in the art.

(h) The Quantity of Experimentation Needed

As discussed at length above, the specification provides exemplary amino acid sequences of AFTI-like polypeptides, extensive guidance regarding conservative amino acid substitutions, and assays for measuring the inhibition of TNF and IL-1 production by monocytes. The amount of experimentation needed is therefore, minimal, and moreover, is routine in the art. As noted in the M.P.E.P., "'[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is

merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" M.P.E.P. § 2164.06, *citing In re Wands*, 858 F.2d at 737. Here, the experimentation is both routine and the specification provides ample guidance for making conservative amino acid substitutions.

(f) The Amount of Direction Provided

As stated in the M.P.E.P. § 2164.03, "[t]he amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." The M.P.E.P. further states that "[t]he 'amount of guidance or direction' refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention." *Id.*

The specification as-filed provides extensive guidance concerning conservative amino acid substitutions that may be made to an AFTI-like polypeptide, so that the polypeptide retains the required activity of inhibiting TNF or IL-1 production by monocytes. The specification devotes at least eight full pages, beginning on page 23, line 17, continuing through page 31, line 17, to a discussion of conservative amino acid substitutions that may be made to the amino acid sequence of SEQ ID NO:2 to produce AFTI-like polypeptides having functional and chemical characteristics similar to those of naturally occurring AFTI polypeptide. In addition, a lengthy table provides exemplary and preferred amino acid substitutions of native amino acid residues with nonnative residues (Table 1, page 25).

The specification further discusses characteristics shared by groups of amino acids, such as side chain properties, hydropathic index, and hydrophilicity, and

discusses how those shared characteristics are used to make conservative substitutions. Specification at pages 26-27. Moreover, the specification discusses how to compare AFTI-like polypeptide sequences with those of related polypeptides using, for example, certain computer algorithms to "identif[y] suitable areas of the molecule that may be changed without destroying activity." *Id*. at pages 27-31. Accordingly, the specification as-filed provides extensive guidance or direction concerning conservative amino acid substitutions that may be made to an AFTI-like polypeptide, so that the polypeptide retains the required activity of inhibiting TNF or IL-1 production by monocytes.

The discussion above demonstrates that the specification is fully enabled for AFTI-like polypeptides having one or more conservative amino acid substitutions, wherein the polypeptide inhibits TNF or IL-1 production by monocytes. The Examiner alleged that "there is insufficient guidance as to the structure of any [AFTI-like polypeptide] fragment having one or more conservative substitution. . . ." Office Action at 8. But "[t]he amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." M.P.E.P. § 2164.03. And, as shown above, Appellants provided extensive guidance or direction concerning conservative amino acid substitutions in the specification as filed. In addition, the amount of knowledge in the state of the art for both apo-A-I and conservative amino acid substitutions is high, as is the level of predictability in the art of conservative amino acid substitutions. Therefore, the specification as filed fully enables one skilled in the art to make and use AFTI-like polypeptides having conservative amino acid substitutions.

All of the *Wands* factors clearly support the conclusion that the claimed invention is fully enabled by the specification. The rejection of claims 9, 10, 15, 16, 36-43, and 46-49 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification is incorrect and should be withdrawn.

Conclusion

For the reasons given above, pending claims 9, 10, 15, 16, 36-43, and 46-49 are allowable and reversal of the Examiner's rejection of these claims is respectfully requested.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Appeal Brief, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 that are not enclosed herewith, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: January 27, 2006

By: _____
William L. Strauss
Reg. No. 47,114

Claims Appendix to Appeal Brief Under Rule 41.37(c)(1)(viii)

1 (withdrawn). An isolated nucleic acid molecule consisting essentially of a nucleotide sequence selected from:

(a) the nucleotide sequence as set forth in residues 73 to 601 in SEQ ID NO:1;

(b) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 194 in SEQ ID NO:2;

(c) the nucleotide sequence as set forth in residues 73 to 451 in SEQ ID NO:1;

(d) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 144 in SEQ ID NO:2;

(e) the nucleotide sequence as set forth in residues 485 to 820 in SEQ ID NO:1;

(f) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 113 in SEQ ID NO:2;

(g) a nucleotide sequence encoding the polypeptide as set forth in residues 73 to 113 in SEQ ID NO:2;

(h) a nucleotide sequence encoding the polypeptide as set forth in residues 156 to 267 in SEQ ID NO:2;

(i) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of at least one of (a) to (f), wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2; and

(j) a nucleotide sequence complementary to at least one of (a)-(h).

2 (withdrawn). An isolated nucleic acid molecule consisting essentially of a nucleotide sequence selected from:

(a) a nucleotide sequence consisting essentially of a nucleotide sequence that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99 percent identical to the nucleotide sequence according to claim 1, wherein the nucleotide sequence encodes a polypeptide that has an activity of the polypeptide as set forth in SEQ ID NO:2;

(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence according to claim 1, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2;

(c) a nucleotide sequence selected from at least one of (a) and (b) encoding a polypeptide of at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2;

(d) a nucleotide sequence selected from at least one of (a), (b), and (c) comprising a fragment of at least about 16 nucleotides; and

(e) a nucleotide sequence complementary to any of (a), (b), or (c).

3 (withdrawn). A vector comprising the nucleic acid molecule of claim 1 or claim 2.

4 (withdrawn). A host cell comprising the vector of Claim 3.

5 (withdrawn). The host cell of Claim 4 which is a eukaryotic cell.

6 (withdrawn). The host cell of Claim 4 which is a prokaryotic cell.

7 (withdrawn). A process of producing an apo-A-1 fragment T-cell activation inhibitor-like polypeptide comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide and isolating the polypeptide from the culture.

8 (withdrawn). A process of producing an apo-A-1 fragment T-cell activation inhibitor-like polypeptide comprising culturing the host cell of Claim 6 under suitable conditions to express the polypeptide and isolating the polypeptide from the culture.

9 (previously presented). A process for making an apo-A-I fragment T-cell activation inhibitor-like polypeptide fragment comprising culturing a eukaryotic cell comprising a vector comprising a nucleic acid molecule consisting essentially of a nucleotide sequence selected from:

(a) the nucleotide sequence as set forth in residues 73 to 582 in SEQ ID NO:1;

(b) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 194 in SEQ ID NO:2;

(c) the nucleotide sequence as set forth in residues 73 to 432 in SEQ ID NO:1;

(d) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 144 in SEQ ID NO:2;

(e) the nucleotide sequence as set forth in residues 466 to 801 in SEQ ID NO:1;

(f) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 113 in SEQ ID NO:2;

(g) a nucleotide sequence encoding the polypeptide as set forth in residues 73 to 113 in SEQ ID NO:2;

(h) a nucleotide sequence encoding the polypeptide as set forth in residues 156 to 267 in SEQ ID NO:2;

(i) a nucleotide sequence complementary to at least one of (a)-(h); and

(j) a nucleotide sequence encoding a polypeptide as set forth in (a) to (h) having one or more conservative amino acid substitutions, wherein the polypeptide inhibits tumor necrosis factor (TNF) or interleukin-1 (IL-1) production by monocytes;

wherein a culture condition suitable for expressing the polypeptide is selected and the polypeptide is isolated from the culture.

10 (previously presented). A process for making an apo-A-I fragment T-cell activation inhibitor-like polypeptide fragment comprising culturing a prokaryotic cell comprising a vector comprising a nucleic acid molecule consisting essentially of a nucleotide sequence selected from:

(a) the nucleotide sequence as set forth in residues 73 to 582 in SEQ ID NO:1;

(b) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 194 in SEQ ID NO:2;

(c) the nucleotide sequence as set forth in residues 73 to 432 in SEQ ID NO:1;

(d) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 144 in SEQ ID NO:2;

(e) the nucleotide sequence as set forth in residues 466 to 801 in SEQ ID NO:1;

(f) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 113 in SEQ ID NO:2;

(g) a nucleotide sequence encoding the polypeptide as set forth in residues 73 to 113 in SEQ ID NO:2;

(h) a nucleotide sequence encoding the polypeptide as set forth in residues 156 to 267 in SEQ ID NO:2;

(i) a nucleotide sequence complementary to at least one of (a)-(h); and

(j) a nucleotide sequence encoding a polypeptide as set forth in (a) to (h) having one or more conservative amino acid substitutions, wherein the polypeptide inhibits tumor necrosis factor (TNF) or interleukin-1 (IL-1) production by monocytes;

wherein a culture condition suitable for expressing the polypeptide is selected and the polypeptide is isolated from the culture.

11 (withdrawn). The process of Claim 7, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for native apo A-1 operatively linked to the DNA encoding the AFTI polypeptide.

12 (withdrawn). The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for native apo A-1 operatively linked to the DNA encoding the AFTI polypeptide.

13 (withdrawn). The isolated nucleic acid molecule according to Claim 2 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

14 (withdrawn). A process for determining whether a compound inhibits AFTI polypeptide activity or production comprising exposing a cell according to claim 4 to the compound, and measuring AFTI polypeptide activity or production in said cell.

15 (previously presented). An isolated apo-A-I fragment T-cell activation inhibitor-like polypeptide fragment consisting essentially of an amino acid sequence selected from: (a) an amino acid sequence as set forth in residues 25 to 194 of SEQ ID NO:2; (b) an amino acid sequence as set forth in residues 25 to 144 of SEQ ID NO:2; (c) an amino acid sequence as set forth in residues 156 to 267 of SEQ ID NO:2; (d) an

amino acid sequence as set forth in residues 25 to 113 of SEQ ID NO:2; (e) an amino acid sequence as set forth in residues 73 to 113 of SEQ ID NO:2; and (f) a polypeptide as set forth in (a) to (e) having one or more conservative amino acid substitutions, wherein the polypeptide inhibits tumor necrosis factor (TNF) or interleukin-1 (IL-1) production by monocytes.

16 (previously presented). An isolated apo-A-1 fragment T-cell activation inhibitor-like polypeptide fragment encoded by a nucleic acid molecule consisting essentially of a nucleotide sequence selected from:

(1) the nucleotide sequence as set forth in residues 73 to 582 in SEQ ID NO:1;

(2) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 194 in SEQ ID NO:2 or the polypeptide as set forth in residues 25 to 194 in SEQ ID NO:2 having one or more conservative amino acid substitutions;

(3) the nucleotide sequence as set forth in residues 73 to 432 in SEQ ID NO:1;

(4) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 144 in SEQ ID NO:2 or the polypeptide as set forth in residues 25 to 144 in SEQ ID NO:2 having one or more conservative amino acid substitutions;

(5) the nucleotide sequence as set forth in residues 466 to 801 in SEQ ID NO:1;

(6) a nucleotide sequence encoding the polypeptide as set forth in residues 25 to 113 in SEQ ID NO:2 or the polypeptide as set forth in residues 25 to 113 in SEQ ID NO:2 having one or more conservative amino acid substitutions;

(7) a nucleotide sequence encoding the polypeptide as set forth in residues 73 to 113 in SEQ ID NO:2 or the polypeptide as set forth in residues 73 to 113 in SEQ ID NO:2 having one or more conservative amino acid substitutions;

(8) a nucleotide sequence encoding the polypeptide as set forth in residues 156 to 267 in SEQ ID NO:2 or the polypeptide as set forth in residues 156 to 267 in SEQ ID NO:2 having one or more conservative amino acid substitutions;

wherein the nucleotide sequence encodes a polypeptide that inhibits tumor necrosis factor (TNF) or interleukin-1 (IL-1) production by monocytes.

17 (canceled).

18 (withdrawn). An antibody produced by immunizing an animal with the polypeptide according to claim 15.

19 (withdrawn). An antibody or fragment thereof which specifically binds the polypeptide according to claim 15.

20 (withdrawn). The antibody according to claim 18 which is a monoclonal antibody.

21 (withdrawn). A hybridoma that produces the monoclonal antibody according to claim 20.

22 (withdrawn). The antibody of claim 18 which is a humanized antibody.

23 (withdrawn). The antibody according to claim 19 which is a fully human antibody or a fragment thereof.

24 (withdrawn). The antibody according to claim 19 which is a chimeric antibody or fragment thereof.

25 (withdrawn). The antibody according to claim 19 which is a CDR-grafted antibody or fragment thereof.

26 (withdrawn). The antibody of claim 19 which is an antiidiotypic antibody or fragment thereof.

27 (withdrawn). The antibody of claim 19 which is bound to a detectable label.

28 (withdrawn). The antibody of claim 19 which is a phage display antibody or fragment thereof.

29 (withdrawn). A method of detecting or quantifying the amount of AFTI polypeptide in a sample comprising contacting the sample with the antibody or fragment according to claim 18 and measuring the antibody - polypeptide interaction.

30 (withdrawn). A selective binding agent or fragment thereof which specifically binds at least one polypeptide according to claim 15.

31 (withdrawn). The selective binding agent according to claim 30 which is a variable region fragment.

32 (withdrawn). The selective binding agent according to Claim 31, wherein the variable region fragment is a Fab or a Fab' fragment.

33 (withdrawn). The selective binding agent according to claim 30 which is bound to a detectable label.

34 (withdrawn). The selective binding agent according to claim 30 which antagonizes AFTI polypeptide biological activity.

35 (withdrawn). A method for treating, preventing, or ameliorating a disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to Claim 30.

36 (original). A composition comprising the polypeptide according to claim 15 and a pharmaceutically acceptable formulation agent.

37 (original). A composition comprising the polypeptide according to claim 16 and a pharmaceutically acceptable formulation agent.

38 (original). The composition according to claim 36, wherein the pharmaceutically acceptable formulation agent comprises at least one of a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

39 (original). The composition according to claim 37, wherein the pharmaceutically acceptable formulation agent comprises at least one of a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

40 (original). The polypeptide according to claim 15, which is covalently modified with a water-soluble polymer.

41 (original). The polypeptide according to claim 40, wherein the water-soluble polymer is selected from polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.

42 (original). The polypeptide according to Claim 16, which is covalently modified with a water-soluble polymer.

43 (original). The polypeptide according to claim 42, wherein the water-soluble polymer is selected from at least one of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.

44 (withdrawn). A viral vector comprising the nucleic acid molecule according to claim 1.

45 (withdrawn). A viral vector comprising the nucleic acid molecule according to claim 2.

46 (previously presented). A fusion polypeptide comprising the polypeptide according to claim 15 and a heterologous amino acid sequence selected from an IgG constant domain or fragment thereof, an alkaline phosphatase or a fragment thereof, a *tat* protein, or a FLAG epitope.

47 (original). The fusion polypeptide according to claim 46, wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

48 (previously presented). A fusion polypeptide comprising the polypeptide according to claim 16 and a heterologous amino acid sequence selected from an IgG constant domain or fragment thereof, an alkaline phosphatase or a fragment thereof, a *tat* protein, or a FLAG epitope.

49 (original). The fusion polypeptide according to claim 48, wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

50 (withdrawn). A method for reducing inflammation in a subject comprising administering to said subject the polypeptide according to claim 15.

51 (withdrawn). A method for reducing inflammation in a subject comprising administering to said subject the polypeptide according to claim 16.

52 (withdrawn). A method for reducing IL-1β secretion in a subject, comprising administering to said subject the polypeptide according to claim 15.

53 (withdrawn). A method for reducing IL-1β secretion in a subject, comprising administering to said subject the polypeptide according to claim 16.

54 (withdrawn). A method for reducing TNF-α secretion in a subject, comprising administering to said subject the polypeptide according to claim 15.

55 (withdrawn). A method for reducing TNF-α secretion in a subject, comprising administering to said subject the polypeptide according to claim 16.

56 (withdrawn). A method for treating an IL-1 mediated disease, comprising administering to said subject the polypeptide according to claim 15.

57 (withdrawn). A method for treating an IL-1 mediated disease, comprising administering to said subject the polypeptide according to claim 16.

58 (withdrawn). A method for treating a TNF-α mediated disease, comprising administering to said subject the polypeptide according to claim 15.

59 (withdrawn). A method for treating, preventing, or ameliorating a medical condition involving monocyte activation, said method comprising administering to a subject a molecule selected from at least one of (a) apo-A-I, (b) an apo-A-1 fragment T cell activation inhibitor (AFTI), and (c) a fusion protein comprising SEQ ID NO: 2.

60 (withdrawn). The method of claim 59, wherein the AFTI is a polypeptide according to claim 15.

61 (withdrawn). The method of claim 59, wherein the AFTI is a polypeptide according to claim 16.

Evidence Appendix to Appeal Brief Under Rule 41.37(c)(1)(ix)

Appellants rely on no evidence in this appeal.

Related Proceedings Appendix to Appeal Brief Under Rule 41.37(c)(1)(x)

Appellants cite no related proceeding decisions in this appeal.